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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,251	11/01/2001	Robert K. Naviaux	UCSD1140-1	9760

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
05/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/889,251	NAVIAUX, ROBERT K.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2-5-08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67,70,73-81,84-91 and 95-145* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67,70,73-81,84-91,101-103, 111-129, 136-138* is/are rejected.

7)☒ Claim(s) *95-100,104-110,130-135 and 139-145* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's Response filed February 5, 2008 is acknowledged. Claims 146-180 are canceled. Claims 67, 70, 73-81, 84-91 and 95-145 remain under consideration.

Those rejections set forth in the last Office Action that are not herein reiterated are withdrawn. The following rejections are the only rejections presently applied to the instant claims

Claims 67, 70, 73-81, 84-91, 101-103, 111-129 and 136-138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 67, 91, 111 and 129 recite mitochondrial disorders that include renal tubular acidosis, lactic academia, 3-hydroxybutyric academia, 1+proteinuria, aminoaciduria and hydroxyprolinuria. The claims lack clarity because these recited disorders characterize numerous disease states and are often more properly considered secondary disorders. For example, hydroxyprolinuria is a finding associated with mental retardation. The Merck Manual is cited – for evidentiary purposes only - to show there are many causes of renal tubular acidosis, lactic academia, 1+proteinuria and aminoaciduria. While MARIAHS syndrome, for example, is known in the art as a "mitochondrial disease," lactic academia is associated with multiple pathologies, such as certain malignancies, AIDS, renal failure, alcohol or drug intoxication and diabetes, for example. The claims are given their broadest, reasonable interpretation.

Clarification is required as to those mitochondrial disorders contemplated, as compared to conditions that are not primary mitochondrial diseases, but rather are findings associated with many distinct disease states.

Clarification is also requested with respect to claims 101-103 as to whether or not MARIAHS syndrome could be the result of prior or concurrent administration of a pharmaceutical agent.

Claims 67, 70, 73-81, 84-91, 96-109 and 111-179 were rejected under 35 U.S.C. 103(a) as being unpatentable over Nagley et al., U.S. Patent 5,981,601, in view of Page et al., Proc. National Academy of Sciences, in the last Office Action. It was asserted Nagley teaches the administration of uridine, including functional derivatives and/or precursors thereof, to treat mitochondrial disorders wherein at least one mutation in the mitochondria has occurred. Nagley's teaching is drawn to the mitochondrial toxicity and physiologic effects that result from the administration of the of the reverse transcriptase inhibitor drug AZT. AZT acts as a mitochondrial poison in that it causes cellular cytotoxicity. As a mitochondrial poison, AZT disrupts mitochondrial respiratory chain function resulting in a reduced capacity for generating ATP. Specifically, AZT affects the oxidation/phosphorylation system and the activity of complex I and IV of the mitochondrial respiratory chain. Further, other diseases associated with disruption of the mitochondrial respiratory chain function are also included in Nagley's teaching. See column 8, line 63, to column 9, line 10, where lactic acidosis is included among those mitochondrial pathologies contemplated. As required by instant claims 88, 89, 107 and 108, see column 7, lines 3-5, where the disclosed daily dosage range overlaps with those instantly claimed. The claimed recitation "about 2 gm/m^2 overlaps with Nagley's teaching of 2000 mg per day.

Functional limitations are recited in instant claims 74-79, 84, 96-100, 102 and 103. The claims are drawn to deficiencies of cardiolipin, of a pyrimidine synthetic pathway, of the uridine synthetic pathway, of the expression and/or activity of an enzyme in the pyrimidine synthetic pathway, such as dihydroorotate dehydrogenase or uridine monophosphate synthetase, and of lower than normal uridine levels. In the absence of a showing that these mechanisms of action are not present in a mitochondrial disorder, one skilled in the art would have considered such deficiencies to be inherent in the pathogenesis of disease processes. Page teaches the safe and effective administration of higher doses of uridine that approach about 6.0 g/m^2.

Claims 146-180 are canceled. The rejection of record under 35 U.S.C. 103 of claims 96-109 and, particularly subsequent to the amendments to claims 111 and 129, of claims 111-145, is withdrawn.

Applicant argues the references fail to teach all of the limitations recited in the claims. Applicant urges the specific diseases or conditions recited in claims 67 and 91 are not disclosed by the cited art.

Nagley's teaching includes treatment directed to lactic acidosis, as well as therapy directed to the mitochondrial effects of AZT. The open language of claims 67 and 91 allows for the administration of multiple therapeutic agents.

The rejection of record of claims 67, 70, 73-81 and 84-91 under 35 U.S.C. 103(a) as being unpatentable over Nagley et al., U.S. Patent 5,981,601, in view of Page et al., Proc. National Academy of Sciences, is maintained for the reasons of record.

No claim is allowed.

Those claims drawn specifically to the treatment of MARIAHS syndrome appear to be free of the prior art.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614

May 7, 2008